CASE REPORT

Coinfection and delayed diagnosis of visceral leishmaniasis: Died predecessors factors

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ABSTRACT

Visceral leishmaniasis (VL) is an anthropozoonosis caused by Leishmania infantum in most Brazilian states and is known for its significant lethality resulting from improper diagnosis and treatment. VL is difficult to diagnose because its clinical manifestations and laboratory abnormalities are analogous to several other pathologies. We report a case of a 54-year-old man, negative for Human Immunodeficiency Virus (HIV), with VL who was initially diagnosed with anemia, consumptive syndrome, pneumonia, chronic obstructive pulmonary disease, and septic shock and died due to a delayed diagnosis of VL.

Key Words: Diagnosis, Low immunity, Clinic bacterial sepsis, Clinical manifestations

1. INTRODUCTION

Visceral leishmaniasis (VL) is one of the six most neglected tropical diseases worldwide, and it is a significant public health problem in several regions of the world.[1] Its occurrence is potentially fatal especially when undiagnosed and treated early, being the second largest cause of death by parasites in the world, after malaria.[2]

The most frequent clinical manifestations include chronic fever, paleness, anorexia, inappetence, hepatosplenomegaly, cough and diarrhea. In some cases infected individuals may be oligo-symptomatic carriers because they have few clinical manifestations, which is a bias for diagnosis since they may be confused with other diseases.[3] For the diagnosis must be considered epidemiological, clinical and laboratory aspects.[2] The hematological and biochemical abnormalities predictive of the disease refer to anemia, thrombocytopenia, leukopenia and hypergammaglobulinemia.[4]

In this context, the present study aimed to report a VL human case with severe immunosuppression and malnutrition, multiresistant bacterial pneumonia, exacerbated chronic obstructive pulmonary disease, septic shock, Leishmania dissemination and death, as a consequence of the late diagnosis of VL, in Dourados Municipality, Brazil, classified as an moderate transmission zone of VL.

2. CASE PRESENTATION

A 54-year-old man was admitted to a public hospital on May 22, 2017, with symptoms of anemia resulting from daily nasal epistaxis for approximately 2 years and presence of intranasal vessels. He had hypertension and was a smoker

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since the age of 14 years. He lost 26 kg of body weight in < 1 year due to the loss of appetite. He was prescribed an anti-hemorrhagic drug, tranexamic acid, at a dose of 1.5 g/day to manage the nasal bleeding.

Eight months later, the patient was for respiratory difficulty, hemoptysis and pulmonary spasms, overall poor condition, and loss of appetite with significant weight loss. Due to suspicions of pulmonary tuberculosis (PT), were examined using the Ziehl-Neelsen method; however, the results were negative. Laboratory findings indicated anemia, leukopenia, and thrombocytopenia. His urea and creatinine levels were 156.0 mg/dl and 1.9 mg/dl, respectively. Two units of packed red blood cells were transfused, and ceftriaxone and levofloxacin antibiotic therapy was initiated. Nonetheless, his pulmonary infection worsened, leading to hemodynamic instability, pallor, dehydration, pulmonary auscultation, vesicular murmurs, sparse snores, and painless palpation without visceromegaly. His extremities showed unclassified edemas, but no signs of deep vein thrombosis.

The patient was transferred to the intensive care unit, required mechanical ventilation of the orotracheal tube because of acute respiratory failure. He presented with hypotension, tachycardia, no fever and acyanosis. He was suspected to have exacerbated chronic obstructive pulmonary disease. His subsequent laboratory tests during the hospitalization suggested an infectious disease (see Table 1). However, nasal and rectal swabs and blood and urine cultures showed the absence of microorganisms. The patient experienced febrile episodes from the 4st to the 11th hospitalization day, even with the use of broad-spectrum antibiotics (ceftriaxone and clarithromycin from the 1st to the 4th hospitalization day, piperacillin/tazobactam and teicoplanin from the 4th to the 12th hospitalization day). Radiography of the anteroposterior chest showed bilaterally ill-defined alveolar opacities, but the cardiac area showed normal patterns and the mediastinum and pulmonary filaments showed no signs of nodules or masses. Chest computed tomography showed several changes (see Figure 1). The diagnosis of PT was again rejected based on the results of 2 smear microscopy tests of tracheal secretions and the diagnosis of Human Immunodeficiency Virus (HIV) I and II was rejected based on the results of antibody tests performed using the rapid test.

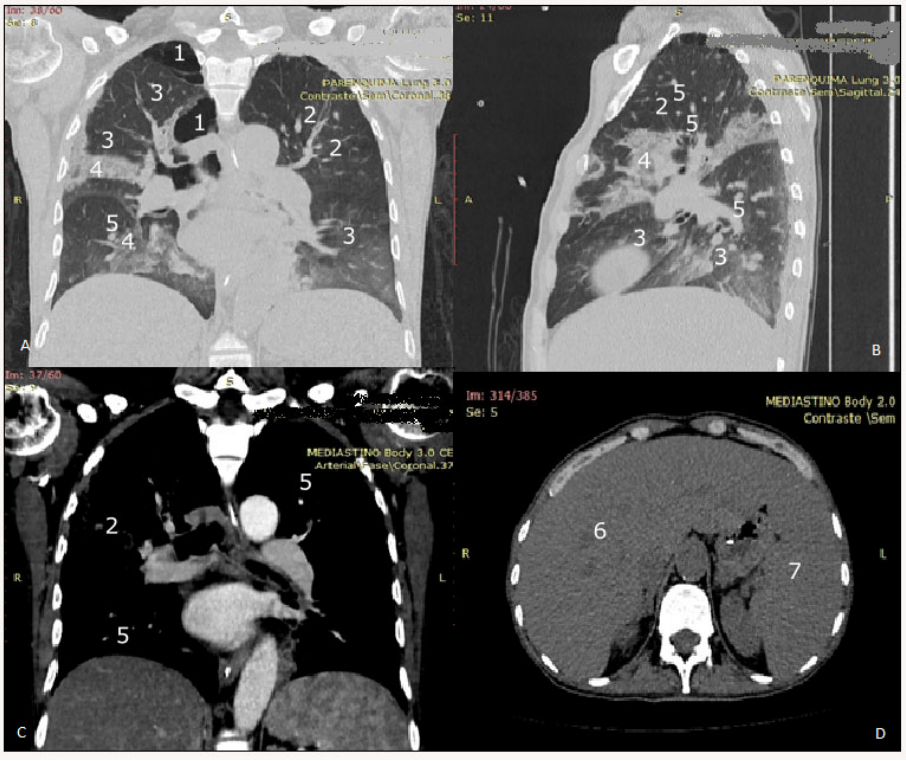

Figure 1. Chest computed tomography, with technique of volumetric acquisition of the data in a multidetector device, with posterior reconstructions, performed on the seventh day of hospitalization. 1) emphysematous blisters; 2) multiple noncalcified centrilobular nodular "budding diffuse" opacities; 3) irregular areas with frosted glass attenuation; 4) pulmonary parenchyma with diffusely heterogeneous density, which assumed a mosaic perfusion pattern; 5) multiple lymph nodes of borderline dimensions in the mediastinum; and enlargement of the right pulmonary hilum, which measured approximately 1.7 × 1.5 cm; 6) hepatomegaly; 7) splenomegaly.

Table 1. Laboratory examinations of the patient during hospitalization days in an intensive care unit (from January 24 to February 3, 2018).

Parameter	Reference values	Days of hospitalization										
		1	2	3	4	5	6	7	8	9	10	11
Hemoglobin	14-16 g/dl	6.40	6.60	6.80	6.70	8.50	8.70	8.20	8.80	8.10	8.70	8.40
Hematocrit	40%-54%	20.40	21.60	22.00	22.90	28.00	28.20	26.70	29.30	26.28	27.80	28.90
MCV	82-92 fl	87.55	89.25	89.43	89.80	90.03	89.52	88.41	90.71	88.74	85.80	91.16
MCH	27 -32 pg	27.46	27.27	27.64	26.27	27.33	27.61	27.15	27.40	26.82	26.85	26.49
MCHC	32 -36 g/dl	31.37	30.55	30.90	29.25	30.35	30.85	30.71	30.03	30.22	31.29	29.06
RDW	11%-15%	17.40	17.50	17.80	18.10	17.00	17.40	17.40	17.80	17.90	17.50	17.90
WBC	5,000-10,000/mm³	3,330	2,900	3,110	3,900	3,570	4,230	4,960	16,070	17,690	4,420	7,520
Platelets	150,000-450,000/mm³	82,000	81,000	97,000	95,000	95,000	79,000	64,000	68,000	76,000	71,000	78,000
TAP	9.8-12.1”	14.1	-	-	-	-	-	-	-	-	-	18.5
TTPA	<33.0”	31.3	-	-	-	-	-	-	-	-	-	36.3
Na+	136-145 mmol/L	131.95	135.47	138.37	139.68	137.85	137.95	141.97	138.14	134.93	135.13	129.89
K+	3.5-5.5 mmol/L	3.62	4.08	4.01	3.98	4.53	4.44	4.21	5.24	5.30	3.77	4.52
Ca++	8.6-10.2 mg/dl	7.9	7.8	7.80	7.9	8.50	8.1	7.8	9.00	8.60	9.10	8.40
Mg++	1.7-2.6 mg/dl	1.87	2.04	2.22	2.25	2.45	2.35	2.45	2.70	2.64	2.22	2.37
Urea	10-50 mg/dl	137.2	154.3	183.8	167.00	174.90	199.20	269.40	338.00	274.90	169.10	128.5
Creatinine	0.5-1.2 mg/dl	2.01	1.82	1.95	1.84	2.57	2.56	3.70	5.78	5.51	4.19	4.01
C-reactive protein	0-5.0 mg/L	39.9	71.0	68.6	148.1	147.80	-	-	-	-	-	-
Direct bilirubin	<0.3 mg/dl	0.15	-.	-	-	-	0.20	-	-	-	-	0.69
Indirect bilirubin	<1.0 mg/dl	0,63	-	-	-	-	0.70	-	-	-	-	0.42
AST (TGO)	<40 U/L	32.6	-	-	-	-	-	-	-	-	-	42.70
ALT (TGP)	<41 U/L	16.9	-	-	-	-	-	-	-	-	-	12.40
Total proteins	6.5-8.7 g/dl	-	-	-	-	-	9.60	-	-	-	-	7.70
Albumin	3.5-5.0 g/dl	2.23	-	-	-	-	2.40	-	-	-	-	1.60
Globulin	2.0-4.0 g/dl	-	-	-	-	-	7.20	-	-	-	-	6.10

Note .MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean concentration of corpuscular hemoglobin; RDW: red cell distribution range; WBC: white blood cell count; TAP: prothrombin time; APTT: activated partial thromboplastin time; AST: aspartate aminotransferase; TGO: glutamic-oxalacetic transaminase; ALT: alanine aminotransferase; TGP: glutamic-pyruvic transaminase.

In the last week of hospitalization, hemogram showed anisocytosis (++), hypochromia (+), polychromasia (+), red cells in rouleaux formation, and cytoplasmic inclusions in blood neutrophils (++), confirming amastigote forms that are suggestive of Leishmania spp. The patient was started on intravenous antibiotic therapy with liposomal amphotericin B (3 mg/kg body weight) for 2 consecutive days, still presented tracheal secretion culture showed the presence of multiresistant Acinetobacter baumannii that was sensitive only to colistin. A subsequent hemoculture was positive for Moraxella (Branhamella) catarrhalis with 2 positive samples in a span of 5 h. The patient died on the 12th hospitalization day in the intensive care unit (2nd day of VL treatment) due to malnutrition, pneumonia, chronic obstructive pulmonary disease, shock septic, and VL. One the day after the patient died, the diagnosis of VL was confirmed in the laboratory by reactive indirect immunofluorescence (titer $\geq$ 1:160) and direct testing of the bone marrow aspirate, which showed amastigotes of Leishmania.

3. Discussion

Owing to its clinical similarities with other diseases, VL diagnosis was delayed in this patient. This case serves as a warning to health professionals. It is essential to consider VL in patients with a history of fever, weight loss, cough, abdominal pain, anemia, pancytopenia, and hypergammaglob-

ulinemia,[3,4] including in regions with low and moderate transmission of VL. Failure to diagnose VL can lead to serious consequences such as the risk of transmission, exposure of patients to unnecessary procedures and diagnoses, and even death. Diagnosis may be delayed due to low sensitivity of the tests and the absence of clinical suspicion. In our case, the clinical signs and laboratory evidence were not noticed, suggesting the need for health care professionals to be more careful.

The high parasitemia, reflected by the presence of the parasite in peripheral blood, suggested that Leishmania dissemination was strongly related to the disease severity due to the lack of specific treatment and late diagnosis. The opportunistic condition caused by high parasitemia was responsible for the growth of multiresistant microorganisms and septic shock, which was evident by the presence of fever, tachycardia, leucopenia, anemia, and thrombocytopenia.[3,5] Immunosuppression concomitant with underlying immunosuppressive diseases is a determining factor of the prognosis of VL.[1] It is important to emphasize that despite being a non-HIV patient the high parasitemia in peripheral blood evidences the weakness of the immune system which favored the hospital infection and the clinical complications. The growth of A. baumannii reflected the body's vulnerability[6] and the presence of M. (B.) catarrhalis was responsible for chronic obstructive pulmonary disease.[7]

The increase in the liver size is evident in VL cases. Changes in the size of organs such as the spleen and liver due to VL are caused by hypertrophy and hyperplasia of the macrophage system that constrains the circulation of capillaries, leading to congestion and infarction. Although treatment with liposomal amphotericin B was started because of the severity of the patient's clinical condition and the high toxicity of pentavalent antimonials, the patient death due to malnutrition, pneumonia, chronic obstructive pulmonary disease, septic shock, and VL on the 2nd day of treatment.

In conclusion, it is evident the importance of early diagnosis for endemic diseases in the patient's origin area, even without the characteristic symptoms of the pathology, in order to identify the possible co-infections and their due treatment. It is important to emphasize that neglect in Brazilian public health is the main cause of death, thus necessitating greater preparation of health care professionals.

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CONFLICTS OF INTEREST DISCLOSURE

The authors declare that they have no competing interest.

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